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## Predictors of Outcome of Surgical Management of Bullous Lung Disease

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**Abstract**--Bullous lung disease are associated with COPD. Bullectomy is the main treatment for giant bullae and complicated patients. The aim was to evaluate predictors of outcome of surgical management of bullous lung disease. This was a descriptive prospective study, 40 patients with bullous lung disease had bullectomy. It was accomplished in our University (April 2018 to July 2020). Operative and post-operative variables were noted. Post-operative air leak was related to lung pathology ( $p = 0.006$ ), degree of

the disease on CT chest ( $p = 0.001$ ) and FEV1 / FVC ratio ( $p = 0.009$ ). Regarding ICU stay  $\geq 2$  days, a correlation was noted with medical comorbidities ( $p = 0.037$ ) and surgical technique ( $p = 0.004$ ), while hospital stay  $> 7$  days was linked to lung pathology ( $p = 0.006$ ), degree of the disease on CT chest ( $p = 0.001$ ) and FEV1 / FVC ratio ( $p = 0.009$ ). Patients with diffuse or localized lung disease and decreased respiratory functions had clinical and functional improvement after surgery. Factors as lung pathology and diffuse lung affection were considered as predictors for prolonged air leak  $> 7$  days and hospital stay  $> 7$  days.

**Keywords**---Bullectomy, outcome, bullous lung, predictors, COPD, VATS.

## **Introduction**

Although bullous lung disease is common among smokers and chronic obstructive pulmonary disease patients, no large randomized controlled trials have been performed and so far, there are still controversies regarding absolute indications, contraindications and timing for surgery. Also, the decision of surgery is tailored according to each patient's condition and the technique of surgical intervention. (1,2)

The aim of this study was to evaluate the predictors of outcome of surgery for bullous lung disease by comparing the preoperative and postoperative physical condition, laboratory investigations, radiological imaging and the post-operative findings.

## **Materials and Methods**

### ***Patient selection and indications for surgery***

Our study was a descriptive prospective study including 40 patients having bullous lung disease and underwent bullectomy as a surgical management. The study was done in the Cardio-thoracic surgery department in our University from April 2018 to July 2020, after obtaining the approval of the ethical committee of our university and a written formal consent from all patients.

### ***Inclusion criteria:***

- Presence of bulla (e) occupying at least one third or more of hemithorax. Or,
- Bulla (e) in the presence of symptoms or complications known to be attributable to them, like pneumothorax or recurrent respiratory infections. Or,
- Bullous lung disease in the presence of diffuse parenchymal involvement (emphysematous or non-emphysematous)

**Exclusion criteria:**

- Surgery done for lung volume reduction (LVRS).
- Surgery for primary spontaneous pneumothorax.
- Surgery done primarily for some other lung disease during which bullectomy was also performed (e.g. patients undergoing lobectomy for bronchiectasis who have associated bulla (e) being excised were excluded from the study).

**Patient preparation and data collection**

All patients were subjected to the following:

- History taking: A thorough detailed history was taken regarding age, sex, smoking history, Medical research council (MRC) dyspnea class as well as previous lung surgery.
- Clinical examination: full examination with oxygen saturation measurement.
- Laboratory investigations:
- Resting Electrocardiography (ECG) and Echocardiography.
- Radiological examination:
  - Plain chest X-ray (CXR)
  - Computed Tomography of chest (CT chest): A recent scan (not more than 6 months) is mandatory for better evaluation of emphysematous lung changes, degree of lung compression and exclusion of complications or masses.
- Pulmonary function test (PFT)
- Arterial blood gases (ABG).
- Pre-operative counseling: a brief explanation of the operation and post-operative period was discussed with the patients. All smokers were advised to quit smoking, as well as patients with COPD were advised to optimize their medical treatment and join a pulmonary rehabilitation program.

**Surgical approach**

Bullectomy was performed under general anesthesia via insertion of a double lumen endotracheal tube. Post operatively, patients were extubated and transferred to the recovery room. However, some patients having respiratory distress were transferred to the standby ICU.

A standard postero-lateral thoracotomy or VATS bullectomy were used for bullectomy at one side while for bilateral bullectomy, a median sternotomy was performed.

A pleural procedure was provided as mechanical pleurodesis, parietal pleurectomy or combined to aid decreasing post-operative air leak, risk of spontaneous pneumothorax and prevention of future bullae formation as well.

## Statistical Analysis

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data was summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test. Comparisons between pre-operative and post-operative data were done using paired t test. (3) For comparing categorical data, Chi square ( $\chi^2$ ) test was performed. Exact test was used instead when the expected frequency is less than 5, pre-operative and post-operative data were compared using Marginal Homogeneity test. (4) Multivariate logistic regression was done to detect independent predictors of different outcomes. P-values less than 0.05 were considered as statistically significant.

## Results

The pre-operative, operative and post-operative data of the patients was collected.

### Pre-operative data:

The population distribution of the study presented male predominance (92.5%) of mean age  $49.05 \pm 10.8$ . The preoperative characteristics were summarized in table 1.

Table 1  
Preoperative characteristics

VARIABLES		DATA
Age (years)	Mean $\pm$ SD	49.05 $\pm$ 10.8
	Range	22 – 65
Sex	Male	37 – (92.5%)
	Female	3 – (7.5%)
Smoking	Yes	36 – (90.0%)
	No	4 – (10.0%)
Medical comorbidities	Present	14 – (35.0%)
	Absent	26 – (65.0%)
Underlying lung pathology	Present	30 – (75.0%)
	Grade 1	0 – (0.0%)
	Grade 2	0 – (0.0%)
	Grade 3	12 – (30.0%)
	Grade 4	23 – (57.5%)
MRC dyspnea score	Grade 5	5 – (12.5%)
	Grade 4	23 – (57.5%)
	Grade 3	12 – (30.0%)
Site of bulla(e)	Bilateral	21 – (52.5%)
	Unilateral	19 – (47.5%)
Lung disease	Diffuse	28 – (70.0%)
	Focal	12 – (30.0%)

- Data are expressed as mean  $\pm$  SD or number (%).

Table (2)  
Descriptive analysis of pre-operative PFT and ABG

VARIABLES		MEAN ± SD	RANGE
Pulmonary Function Test (n = 32)	FEV1 (L)	1.45 ± 0.29	0.90 - 2.30
	FVC (L)	2.38 ± 0.33	1.70 - 2.90
	FEV1 / FVC	60.73 ± 6.58	50.00 - 80.00
Arterial Blood Gases (n = 40)	PO <sub>2</sub> (mmHg)	87.60 ± 3.33	80.00 - 93.00
	PCO <sub>2</sub> (mmHg)	35.82 ± 3.62	30.00 - 43.00
	SaO <sub>2</sub> (%)	92.57 ± 2.10	88.00 - 96.00

- Data are expressed as mean ± SD or number (%).

### Operative data

Mean duration of surgery was 99.75 ± 20.19 minutes (range, 60 - 160), longer surgical time was found in patients with median sternotomy approach and those with multiple bullae on the same side. The surgery was one sided in 38 patients and bilateral in 2 (5%). VATS was the surgical approach in 14 (35%). All patients had pleural procedures, in the form of mechanical pleurodesis alone (87.5%) and combined with parietal pleurectomy in 5 (12.5%).

Table 3  
Descriptive analysis of the operative data recorded in the study

VARIABLES		DATA
Duration of surgery (minutes)	Mean ± SD	99.75 ± 20.19
	Range	60 - 160
Side of surgery	Right	20 - (50.0%)
	Left	18 - (45.0%)
	Bilateral	2 - (5.0%)
Surgical technique	Thoracotomy	24 - (60.0%)
	VATS	14 - (35.0%)
	Median sternotomy	2 - (5.0%)
Pleural procedure	Mechanical pleurodesis	35 - (87.5%)
	Parietal pleurectomy	0 - (0.0%)
	Combined	5 - (12.5%)

Data are expressed as mean ± SD or number (%).

### Post-operative data

Post extubation, most patients were transferred to the ward while 12 patients needed ICU for 1 - 2 days with mean ICU stay 0.67 ± 0.33 days, 2 of them having median sternotomy. The post-operative data was collected in the following table.

Table (4)  
Descriptive analysis of post-operative data

VARIABLES		DATA
Bleeding (ml)	Mean $\pm$ SD	273.75 $\pm$ 91.39
	Range	100 - 500
ICU stay (days)	Mean $\pm$ SD	0.67 $\pm$ 0.33
	Range	0 - 2
Hospital stay (days)	Mean $\pm$ SD	8.13 $\pm$ 3.9
	Range	4 - 12
Air leak (days)	Less than 7 days	25 - (62.5%)
	More than 7 days	15 - (37.5%)
Chest tube duration (days)	Mean $\pm$ SD	7.67 $\pm$ 3.49
	Range	4 - 20
MRC dyspnea score	Grade 1	18 - (45.0%)
	Grade 2	20 - (50.0%)
	Grade 3	2 - (5.0%)
	Grade 4, 5	0 - (0.0%)
	Grade 5	0 - (0.0%)
CXR / CT chest full lung expansion		40 - (100.0%)
Discharge on one way valve		3 - (7.5%)
Post-operative mortality		0 - (0.0%)

Data are expressed as mean  $\pm$  SD or number (%).

### Predictors of the outcome

Correlations were done between pre-operative and post-operative variables, aiming to determine possible predictors for the outcomes following bullectomy. Post-operative variables included: prolonged air leak more than 7 days, ICU stay  $\geq$  2 days, hospital stay more than 7 days, post-operative complications and discharge on one way valve. Each of the post-operative variables was correlated to the following pre-operative ones: Age, sex, underlying lung pathology, MRC dyspnea score, medical comorbidities, CT chest (Site of bullae, lung disease and complications), pulmonary function tests (FEV1, FVC, FEV1/FVC) and surgical technique.

Regarding the post-operative prolonged air leak, significant correlation was obvious considering underlying lung pathology ( $p = 0.006$ ), degree of the disease on CT chest ( $p = 0.001$ ) and FEV1 / FVC ratio ( $p = 0.009$ ). While there was no correlation with the rest of the preoperative variables.

Table 5  
Correlation between the post-operative air leak and the pre-operative PFTs

VARIABLES	AIR LEAK		<i>p</i> value
	< 7 DAYS MEAN ± SD	> 7 DAYS MEAN ± SD	
Age (years)	47.64 ± 13.04	51.40 ± 4.87	0.203
FEV1 (L)	1.51 ± 0.35	1.36 ± 0.15	0.102
FVC (L)	2.39 ± 0.36	2.37 ± 0.30	0.912
FEV1 / FVC	62.90 ± 7.62	57.56 ± 2.53	<b>0.009</b>

- Data are expressed as mean ± SD or number (%).
- P > 0.05= not significant (NS)

Table 6  
Correlation between the post-operative air leak and the pre-operative variables

VARIABLES	AIR LEAK		<i>p</i> value
	< 7 DAYS COUNT (%)	> 7 DAYS COUNT (%)	
Sex	Male	22 – (59.5%)	0.279
	Female	3 – (100.0%)	
Underlying lung pathology	Present	15 – (50.0%)	<b>0.006</b>
	Absent	10 – (100.0%)	
MRC dyspnea score	Grade 3	8 – (66.7%)	1
	Grade 4	14 – (60.9%)	
	Grade 5	3 – (60.0%)	
Medical comorbidities	Present	9 – (64.3%)	0.864
	Absent	16 – (61.5%)	
CT Site of bullae	Unilateral	14 – (73.7%)	0.165
	Bilateral	11 – (52.4%)	
CT Chest Lung disease	Localized	12 – (100.0%)	<b>0.001</b>
	Diffuse	13 – (46.4%)	
Pre-operative complications	Present	6 – (54.5%)	0.716
	Absent	19 – (65.5%)	
Surgical technique	Thoracotomy	13 – (54.2%)	0.283
	VATS	11 – (78.6%)	
	Median sternotomy	1 – (50.0%)	

- Data are expressed as mean ± SD or number (%).
- P > 0.05= not significant (NS)

Regarding the ICU stay  $\geq 2$  days, there was a significant correlation with the medical comorbidities ( $p = 0.037$ ) and surgical technique ( $p = 0.004$ ) only.

Table 7  
Correlation between the ICU stay and other variables

VARIABLES		ICU STAY (DAYS)		p value
		< 2 DAYS COUNT (%)	$\geq 2$ DAYS COUNT (%)	
Gender	Male	34 – (91.9%)	3 – (8.1%)	1
Underlying lung pathology	Present	27 – (90.0%)	3 – (10.0%)	0.560
MRC dyspnea score	Grade 3	12 – (100.0%)	0 – (0.0%)	0.059
	Grade 4	22 – (95.7%)	1 – (4.3%)	
	Grade 5	3 – (60.0%)	2 – (40.0%)	
Medical comorbidities	Present	11 – (78.6%)	3 – (21.4%)	0.037
CT Site of bullae	Bilateral	18 – (85.7%)	3 – (14.3%)	0.233
CT Chest Lung disease	Localized	12 – (30.0%)	0 – (0.0%)	0.541
	Diffuse	25 – (69.3%)	3 – (10 %)	
Pre-operative complications	Present	11 – (100.0%)	0 – (0.0%)	0.548
	Thoracotomy	23 – (95.8%)	1 – (4.2%)	
Surgical technique	VATS	14 – (100.0%)	0 – (0.0%)	0.004
	Median sternotomy	0 – (0.0%)	2 – (100.0%)	

- Data are expressed as mean  $\pm$  SD or number (%).
- $P > 0.05$ = not significant (NS)

Table 8  
Correlation between the ICU stay and the pre-operative PFTs

VARIABLES	ICU STAY		p value
	< 2 DAYS MEAN $\pm$ SD	$\geq 2$ DAYS MEAN $\pm$ SD	
Age (years)	48.30 $\pm$ 0.84	58.33 $\pm$ 4.16	0.123
FEV1 (L)	1.48 $\pm$ 0.29	1.22 $\pm$ 0.17	0.147
FVC (L)	2.40 $\pm$ 0.33	2.17 $\pm$ 0.29	0.247
FEV1 / FVC	61.19 $\pm$ 6.74	56.30 $\pm$ 1.25	0.226

- Data are expressed as mean  $\pm$  SD or number (%).
- $P > 0.05$ = not significant (NS)

Regarding the hospital stay > 7 days, it was affected by the underlying lung pathology (COPD) ( $p = 0.006$ ), degree of the disease on CT chest ( $p = 0.001$ ) and FEV1 / FVC ratio ( $p = 0.009$ ).

Table 9  
Correlation between the post-operative hospital stay > 7 days and the pre-operative PFTs

VARIABLES	HOSPITAL STAY > 7 DAYS		<i>p</i> value
	NO	YES	
	MEAN ± SD	MEAN ± SD	
Age (years)	47.64 ± 13.04	51.40 ± 4.87	0.203
FEV1 (L)	1.51 ± 0.35	1.36 ± 0.15	0.102
FVC (L)	2.39 ± 0.36	2.37 ± 0.30	0.912
FEV1 / FVC	62.90 ± 7.62	57.56 ± 2.53	<b>0.009</b>

- Data are expressed as mean ± SD or number (%).
- $P > 0.05$ = not significant (NS)

Table 10  
Correlation between the post-operative hospital stay > 7days and other variables

VARIABLES		HOSPITAL STAY > 7 DAYS		<i>p</i> value
		NO	YES	
		COUNT (%)	COUNT (%)	
Sex	Male	22 – (59.5%)	15 – (40.5%)	0.279
Underlying lung pathology	Present	15 – (50.0%)	15 – (50.0%)	<b>0.006</b>
MRC dyspnea score	Moderate	8 – (66.7%)	4 – (33.3%)	1
	Severe	14 – (60.9%)	9 – (39.1%)	
	At rest	3 – (60.0%)	2 – (40.0%)	
Medical comorbidities	Present	9 – (64.3%)	5 – (35.7%)	0.864
CT Site of bullae	Bilateral	11 – (52.4%)	10 – (47.6%)	0.165
CT Chest Lung disease	Diffuse	13 – (46.4%)	15 – (53.6%)	<b>0.001</b>
Pre-operative complications	Present	6 – (54.5%)	5 – (45.5%)	0.716
Surgical technique	Thoracotomy	13 – (54.2%)	11 – (45.8%)	0.283
	VATS	11 – (78.6%)	3 – (21.4%)	
	Median sternotomy	1 – (50.0%)	1 – (50.0%)	

- Data are expressed as mean ± SD or number (%).

-  $P > 0.05$  = not significant (NS)

Finally, the post-operative complications and discharge on one way valve were not correlated with any of the pre-operative variables.

## Discussion

Regarding bullectomy, many criteria were highlighted to allow better selection of candidates and to avoid high risk patients with high morbidity, mortality or less likely to benefit from surgical intervention, however these criteria were not absolute and variable between different studies. (5)

Our data included 37 males (92.5%) and 3 females (7.5%) and the mean age  $49.05 \pm 10.8$  years old (ranging from 22 – 66), which was similar to the age group of the study performed by Schipper et al. 2004, who reported 43 patients (38 males, 5 females) with mean age  $54 \pm 10$ , and Palla et al. 2005 who reported 41 patients as 36 men and 5 women with mean age  $48.4 \pm 14.8$ .(1,6)

In our study, there was 14 patients (35%) with other medical comorbidities, 10 patients with systemic hypertension and 4 patients with diabetes mellitus. That was similar to Krishnamohan et al. 2014, who also reported 10 patients with diabetes mellitus and 38 patients with hypertension. (7)

Regarding our radiological assessment, the site of bulla(e) was unilateral in 19 patients (47.5%) and bilateral in 21 patients (52.5%), and there was diffuse involvement of underlying lung in 28 patients (70%) and localized disease in 12 patients (30%). In view of this, the data was comparable with Vigneswaran W. et al. 1992, reported that all patients (22) had bullae occupying at least one third of the hemithorax with evidence of peripheral bullae and generalized emphysema as well. Also Baldi et al, 2001, mentioned that bilateral bullae existed in 8 of 25 patients (32%), signs of emphysema in 12 of 25 patients (48%) and signs of compression in 17 patients (68%). Krishnamohan et al. 2014, identified a giant bulla in 53 of 63 patients, with diffuse emphysema in 45 patients (71%), and bullae were unilateral in 55 patients (87%) and bilateral in 8 patients (13%). In addition, Lone YA et al. 2012, Gunnarsson SI et al. 2012 and FitzGerald MX et al. reported similar data as well. (7–12)

## Predictors of the outcome

Pre-operative and post-operative data were correlated in order to determine proper predictors for the outcomes following bullectomy. Regarding the prolonged post-operative air leak (> 7 days) and the hospital stay (> 7 days), All 15 patients with prolonged air leak and hospital stay more than 7 days are known to have underlying pathology (COPD) and diffuse lung disease in the CT chest. Also, prolonged air leak and hospital stay were tightly linked to the pre-operative FEV1/FVC (mean  $57.56 \pm 2.53$ ).

Owing to multivariate regression analysis, underlying pathology, diffuse lung disease and FEV1/FVC were considered as independent predictors for prolonged post-operative air leak and hospital stay. ( $p = 0.006$ ,  $p = 0.001$  and  $p = 0.009$ )

respectively). This can be explained by the fact that, patients with COPD mostly have diffuse bilateral emphysematous lung changes and lower respiratory functions. Furthermore, prolonged air leak was expected in those patients because the diseased lung has poor healing ability and the suture line becomes under tension when the lung expands.

On the other hand, the need for more hospital stay was mainly for monitoring of the air leak, while some of patients required intense physical exercise, chest rehabilitation and wound care.

Regarding the ICU stay  $\geq 2$  days, 3 patients stayed for 2 or more days in the ICU for adequate control of chest condition, maximizing their medical treatment and pain management. Out of the 3 patients, 1 had postero-lateral thoracotomy approach with  $p < 0.004$  and 2 patients had median sternotomy approach due to their pre-operative condition and lung function.

### **Summary and Conclusion**

In this study, evaluation of the predictors of bullous lung disease surgical management outcome was our target. We found that factors as underlying lung pathology (COPD) and diffuse lung affection in the CT chest can be considered as predictors for prolonged post-operative air leak more than 7 days and hospital stay more than 7 days. These patients mostly will need intense post-operative physiotherapy, mobilization and optimization of their medical treatment. Also, patients performed median sternotomy approach are expected to have longer ICU stay, owing to affection of both lungs and the associated pain as well.

### **Limitations:**

- Need for more cases done via VATS, as the technique is becoming a standard.
- The short post-operative follow up duration.

### **Recommendations**

Early diagnosis and surgical management of bullous lung disease with proper pre-operative preparation, accurate surgical technique and intense post-operative care can provide good prognosis and prevent future complications for those patients.

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**TABLES**

<b>Table no.</b>	<b>Title</b>
<b>1</b>	Preoperative characteristics
<b>2</b>	Descriptive analysis of pre-operative PFT and ABG
<b>3</b>	Descriptive analysis of the operative data recorded in the study
<b>4</b>	Descriptive analysis of post-operative data
<b>5</b>	Correlation between the post-operative air leak and the pre-operative PFTs
<b>6</b>	Correlation between the post-operative air leak and the pre-operative variables
<b>7</b>	Correlation between the ICU stay and other variables
<b>8</b>	Correlation between the ICU stay and the pre-operative PFTs
<b>9</b>	Correlation between the post-operative hospital stay > 7 days and the pre-operative PFTs
<b>10</b>	Correlation between the post-operative hospital stay > 7days and other variables

**ABBREVIATIONS**

ABG = arterial blood gases; FEV<sub>1</sub> = forced expiratory volume in first second; FRC = functional Residual Capacity; FVC = forced vital capacity; LVRS = lung volume reduction surgery; PFTs = pulmonary function tests; VATS= video assisted thoracoscopic surgery.